REMARKS/ARGUMENTS

The Office Action mailed December 22, 2005 has been carefully considered and the following response prepared. Claims 14, 18, 20, 21, 24, 30-35 and 40 have been amended. Claims 38 and 39 have been canceled without prejudice.

At page 2 of the Office Action claims 14-26 and 29-40 were rejected under 35 USC 112, first paragraph as failing to comply with the written description requirement.

Part of the instant rejection relates to the Examiner's assertion that the specification does not provide a written description for elements of a gene such as promoters and untranslated regions and thus persons skilled in the art would not recognize that Applicants were in possession of the gene elements of each respective genus of ilvD, ilvBCN, ilvC, panB, panC, panD and panE genes.

Applicants' attorney Liza D. Hohenschutz would like to thank Examiner Fronda for the telephone conference on October 27, 2005 during which the foregoing rejection was discussed. Examiner Fronda explained that "gene" refers not only to a coding region, but also to '5 and '3 regulatory sequences such as promoters, enhancers, and '3-untranlslated regions and that the rejection could be overcome by amending claim 14 to delete gene and substitute nucleotide sequence or polynucleotide encoding the recited ilvD or ilvBNC. Claim 14 has been amended to delete reference to a "gene construct" and state that the microorganism is transformed with a nucleotide sequence encoding ilvD, ilvBNC or both ilvD and ilvBNC.

In the remainder of the rejection, the Examiner asserts that the specification does not provide an adequate written description of ilvD, ilvBNC, panB and other enzymes disclosed in the specification because there is no description of structural features and amino acid sequences commonly possessed by the genus of each enzyme and thus persons skilled in the art cannot visualize or recognize the identity of members of each genus for use in the claimed method.

Applicants traverse this rejection. In the recent case *Capon v. Eschhar*, 76 USPQ2d 1078 (Fed. Cir. 2005), the Federal Circuit held that section 112, does not impose a *per se* rule requiring recitation in the specification of the nucleotide sequences of claimed DNA when that sequence is already known in the filed. The Court added that

the "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. The Court further stated that the descriptive text needed to meet the "written description" requirement varies with the nature and scope of the invention at issue, and with the scientific and technological knowledge already in existence. To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention. In assessing whether Applicants have provided an adequate written description of the invention, the scope and content of the prior art must be taken into consideration.

At the priority date of the present application, the enzymes associated with biosynthesis of the branched chain amino acid valine were well-characterized. This pathway is described, for example, in DeRossi et al., Gene 166: 127-132 (1995). The nucleotide and protein sequences of dihydroxy acid dehydratase (ilvD) were known from sources including *Clostridium pasteurianum* (GenBank Acc. no. L06666), *Schizosaccharomyces pombe* (GenBank acc. no. D89254), *Lactococcus lactis* (GenBank acc. no U92974) and *E. coli* (GenBank acc. no. M10303). The nucleotide and protein sequences of acetohydroxy acid synthase (ilvBN) were known from sources including *Lactococcus lactis* (GenBank acc. no. U92974), *Methanococcus aeolicus* (GenBank acc. no. U35458), *Leuconostoc mesenteroides* (GenBank acc. no. U50749), *Mycobacterium avium* (GenBank acc. no. L49392), *Streptomyces avermitilis* (GenBank acc. no. L39268), *Corynebacterium glutamicum* (GenBank acc. no. L09232) and *Bacillus subtilis* (GenBank acc. no. L03181). Isomeroreductase (ilvC) was known from sources including *Mycobacterium avium* (GenBank acc. no. L49392), *Streptomyces avermitilis* (GenBank acc. no. L39268), *Bacillus subtilis* (GenBank acc. no. L03818), *Corynebacterium glutamicum* (GenBank acc. no. L09232) and *Leuconostoc mesenteroides* (GenBank acc. no. U50749).

Structural features common to ilvD and ilvBNC from various sources was known or could be obtained by a comparison of the sequences. Some of the common features of ilvBN are disclosed in DeRossi *et al.*, and primers based on conserved sequences were used to isolate a further ilvBN sequence from *Streptomyces avermitilis*. Velasco *et al.*,

Gene 137: 179-185 (1993) discloses a comparison of dihydroxy acid dehydratase (i.e., ilvD) from *Lactococcus lactis*, *E. coli* and *Saccharomyces cerevisiae*. At the time of filing of the present application, ilvD and ilvBNC were known from several sources and common structural characteristics correlated with the function of the enzymes was known or could be obtained by simple comparison of the sequences.

Similarly, the enzymes involved with the synthesis of D-pantothenate, ketopantoate hydroxymethyl transferase (panB), pantothenate ligase (panC), ketopantoic acid reductase (panE) and aspartate decarboxylase (panD) were well-characterized. The nucleotide and protein sequence of panB was known from sources including *Helicobacter pylori* (GenBank acc. no. AE001471), *Mycobacterium bovis* (GenBank acc. no. U57435) and *E. coli* (GenBank acc. no. L17086). The nucleotide and protein sequence of panC was known from sources including *Helicobacter pylori* (GenBank acc. no. AE001440), *Synechocystis* sp. (GenBank acc. no. U44896) and *E. coli* (GenBank acc. no. L17086). The nucleotide and protein sequence of panD was known from sources including *Ralstonia eutropha* (GenBank acc no. AF061246), *Helicobacter pylori* (GenBank acc. no. AE001442) and E. coli (L17086). PanE was known, for example, from *Salmonella typhimurium*, *E. coli* and *Bacillus subtilis*.

At the time of filing of the present application, panB, panC, and panD were known from several sources and common structural characteristics correlated with the function of the enzymes was known or could be obtained by simple comparison of the sequences. PanE was also known from several sources.

When the scope and content of the prior art are taken into consideration, as required, Applicants have provided an adequate written description of each enzyme. Withdrawal of the rejection of claims14-26 and 29-40 under 35 USC 112, first paragraph as failing to comply with the written description requirement is requested.

At page 4 of the Office Action, the Examiner rejected claims 14-18, 20-26 and 30-40 under 35 USC 112, first paragraph as not enabled because the specification does not reasonably provide enablement for any embodiment other than transformation with sequences disclosed in the specification. In the present Office Action the Examiner alleged that screening and searching for the genes recited in the claims from additional biological sources with differing nucleotide sequences and structures using functional

complementation is not guidance for making the claimed invention, but is a trial and error type of experimentation requiring undue experimentation. The Examiner further asserted that persons skilled in the art would require additional guidance such as information regarding the specific nucleotide sequence of and biological source of the ilvD or ilvBNC gene.

Applicants traverse this rejection. Patent applicants must disclose their invention with sufficient detail so that persons skilled in the pertinent art can make and use the claimed invention without undue experimentation. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004). Enablement of patent claims is determined by reference to the disclosures of the patent itself and the knowledge of persons skilled in the pertinent art at the time the patent application was filed.

Undue experimentation is not required for persons of ordinary skill in the art to isolate ilvD and ilvBNC genes from other microorganisms. The instant specification provides guidance at pages 6-8 for isolating genes using functional complementation. The method at pages 6-8 of the specification was used to isolate ilvD from *Corynebacterium glutamicum* and can be used to isolate genes from other microorganisms. Additionally, persons skilled the art can use known ilvD and ilvBNC sequences as probes to isolate the corresponding sequences in other microorganisms using techniques known in the art. DeRossi *et al.* discloses the use of primers designed from two highly conserved sequences of acetohydroxy acid synthases to obtain the *Saccharomyces avermitilis* ilvBN gene. Confirmation of the gene was obtained by functional complementation in *E. coli* having an ilv^- mutation. The authors also disclose isolation of ilvC as part of a gene cluster with ilvBN. Gusberti *et al.*, Gene 177: 83-85 (1996) discloses the use of the *Saccharomyces avermitilis* ilvBN gene to isolate the *Mycobacterium avium* ilvBNgene. Velasco *et al.* used probes designed from a highly homologous region of *Lactococcus lactis* and *E. coli* to clone the dihydroxy acid dehydratase gene from *Saccharomyces cerevisiae*. Examples of nucleotide sequences encoding ilvD and ilvBNC that were known at the time the application was filed are discussed above.

The portion of the present rejection relating to an endogenous ilvD gene that will result in increased activity of ilvD is moot in view of the amendment to claim 30 deleting

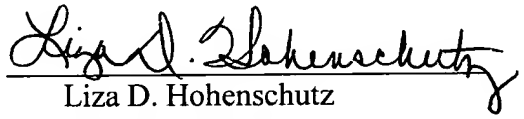
reference to the endogenous ilvD gene. Claim 30 has been amended to state that the activity of dihydroxy acid dehydratase (ilvD) is increased by increased expression of the ilvD nucleotide sequence encoding ilvD.

At the time the present application was filed, persons skilled in the art could readily obtain ilvD and ilvBNC sequences using techniques known in the art such as functional complementation and/or using known ilvD or ilvBNC sequences as probes, as discussed above. The disclosures of the specification allow persons skilled in the art to practice the invention as claimed without undue experimentation. Withdrawal of this section 112, first paragraph rejection is requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is requested and an early Notice of Allowance is earnestly solicited.

Respectfully submitted,
CONNOLLY BOVE LODGE & HUTZ LLP

Date: January 19, 2006

By: 

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